

# PCBs: ICF Status Report

July 30th, 2020



Raquel Silva  
Cynthia Lin  
Joanne Tigoveich  
Steven Black

# Attendance

## \* EPA

- \* Geniece Lehmann
- \* Laura Carlson

## \* ICF

- \* Raquel Silva
- \* Cynthia Lin
- \* Joanne Trgovcich
- \* Steven Black



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## Action Items

Topic	Task	Assigned to	Date Due	Slide #
MIST	Finalize and submit work plan, taking into account discussion of feedback (slide 7)	ICF (Raquel)	8/5/2020	6-7
MIST	EPA to review User Guide and provide feedback	EPA (Geniece)	-	6
ADME	Step 1 – finalize report	ICF (Raquel)	8/14/2020	8
ADME	Step 2 – finalize screening and submit report	ICF (Steven)	8/14/2020	8
ADME	Step 3 – continue extractions	ICF (Steven)	9/18/2020	8
ADME	Update literature flow diagram	ICF (Raquel)	8/28/2020	8
Manuscript	Contact expert authors about outstanding drafts and revisions	ICF (Raquel)	8/7/2020	10/11
Epi Neuro SQE	Coordinate with experts and Kristen about restarting work.	ICF	8/3/2020	11
Reference tagging in litstream	Finalize re-tagging of references in list sent by EPA	ICF (Raquel)	8/5/2020	11



# Major Decisions

## ※ TO-34

### \* Management

- No new decisions made.

### \* Evidence Map Manuscript (TD-003 + TO-09/TD-003)

- Section authors will review new inventories. Only minor edits may be required for most sections.

### \* MiST

- Various decisions about revision of the tool as described in Slide 7

### \* ADME

- Supporting Epi should be treated like Other Supporting in the literature flow diagram. No changes are necessary to the reports.
- Only studies that would otherwise be ADME relevant except for the species should be tagged to the Species Not PECO Relevant category
- Exposure Studies and Species Not PECO are the only supplemental tags that are exclusive; include a comment in the instructions to make this more clear for the next round of screening
- Timeline for next ADME literature update should be similar to last year's: PCBs literature search in September and then a screening for Hazard ID and for ADME in November

## ※ TO-37

### \* Literature screening & developing inventories

- KAT analysis can proceed for food consumption

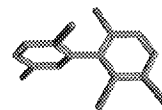


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## Agenda for July 30th, 2020

- § **TO-34**
  - § **TD-003: MiST**
  - § **TD-002: ADME Screening and Extraction**
  - § **TD-001: Evidence Map Manuscript (+TO-09/TD-003)**
- § **Hazard ID (TO-37/TD-003)**
- **Budget Update**



## MIST

### \* **MiST revision**

- \* Revisions complete
- \* Internal QC on hold

### \* **Materials and Methods section for Mixtures Manuscript**

- \* Revision of draft for methods on hold, including preparing literature flow diagram and abstract review of foreign language studies

### \* **User Guide**

- \* User Guide draft submitted on 6/10. Waiting for feedback from EPA.



Now TO-34/TD-003. Work plan in preparation.

**MIST****\* Feedback on tool revision**

- \* Laura run neurological dataset reanalysis using revised tool results and provided comments (email, 7/24)

**\* Major issues:**

- Tool requires a mixture specific ED to run in all scenarios
- Data poor scenario—for mixtures where there is no BMD - tool still requires an ED value
- It's confusing to have a mixture # and a mixture name in the settings tab
- Tool would not accept the mixing ratio inputs in the blue cells unless they were all less than 1 and scaled already to total 1.

**\* Minor issues:**

- Consistency in BMD type in user guide and the data repository
- Excel workbook would not allow opening the "options" page (protected?)
- Sometimes changing/editing the number of reference mixtures in the "settings" tab resulted in no new blue cells auto-appearing
- Not intuitive for entering CDF information
- Copying/pasting doesn't work well in the tool

**Discussion of major issues:**

Tool requires a mixture specific ED to run in all scenarios

Jeff – Include simple test code so that when you hit the run analysis button it checks if you filled in the ED or the critical delta. If you have one or the other it will run, but if neither, then it shows a warning.

Graham: This would be easy to implement.

Data poor scenario—for mixtures where there is no BMD - tool still requires an ED value.

This would also be fixed with the modification discussed in the first bullet

It's confusing to have a mixture # and a mixture name in the settings tab

Laura: Making this more clear in the user guide/quick start guide would be beneficial to improving clarity

Jeff: When you lock or unlock, it asks you which mixture you want, so that number is the number that is on the repository data tab. If this designation of the settings tab could be done the same way, it would ask which mixture of the other tab would you want to use as the reference mixture.

Laura: We could just add a flag to remind users that they should enter the mixture name and not the numbered list that populates

Jeff: Is there any reason why that number even shows up? Could we just have the name show up as blue and not the number?

Conclusion: remove the numbers or use roman numerals, or a similar solution that removes the confusion.

Tool would not accept the mixing ratio inputs in the blue cells unless they were all less than 1 and scaled already to total 1.

Graham: I need to review this.

Laura: Could this be linked to the copy/paste issue within the tool?

Graham: Maybe we need to add a method of adding things to the clipboard

This issue is occurring in both versions that had been sent to EPA (April 2019 and June 2020)

ACTION ITEM: schedule meeting to do screen share so that Graham can observe the issue in action (Jeff, Graham, Joanne and Laura)

Additional issue: There are language inconsistencies in the user guide v. the quick start guide that need to be corrected.





"Does the reference meet the PECO criteria (i.e., Is the reference relevant to ADME)?"


- YES:
  - Is the reference available only as an abstract? Tag "Other Supporting/Abstract only"
  - Is the reference written in a language other than English? Tag "Other Supporting/Non-English Language"
  - Is the reference a secondary data source? Tag "Other Supporting/Secondary Data Source"
  - If the reference is not tagged to abstract only, non-English language, or secondary data source, Tag "Relevant to ADME"
- NO:
  - "Is the reference relevant to the IRIS PCB assessment in any way?"
    - YES: Is the reference a "Supporting Epi Study"?
      - YES:
        - Is the reference available only as an abstract? Tag "Other Supporting/Abstract only"
        - Is the reference written in a language other than English? Tag "Other Supporting/Non-English Language"
        - Is the reference a secondary data source? Tag "Other Supporting/Secondary Data Source"
        - If the reference is not tagged to abstract only, non-English language, or secondary data source, Tag "Supporting Epi Study"
      - NO: Would the reference have met the PECO criteria if it had been conducted in a PECO-relevant species?
        - YES: Tag "Other Supporting/Species not PECO Relevant" and stop tagging
        - NO: Is the reference an "Exposure Study"?
          - YES: Tag "Other Supporting/Exposure Study" and stop tagging
          - NO: Does the reference contain information on "Physical/Chemical Properties" of PCBs?
            - YES: Tag "Other Supporting/Physical/Chemical Properties" and stop tagging
            - NO: Tag "Not Relevant to ADME" and stop tagging
      - NO: Tag "Off Topic" and stop tagging

• **Updated literature flow diagram (ETC: 8/28)**

--- Which tags should be mutually exclusive?

  - **Relevant to ADME**
  - **Not Relevant to ADME (+ Off Topic)**
  - **Supporting Epi Study**
  - **Other Supporting**

Abstract only  
 Foreign Language  
 Secondary Data Source  
 Exposure Study  
 Physical/Chemical Properties  
**Species not PECO Relevant**



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Supporting Epi should be treated like Other Supporting in the literature flow diagram. No changes are necessary to the reports. Only studies that would otherwise be ADME relevant except for the species should be tagged to the Species Not PECO Relevant category

Exposure Studies and Species Not PECO are the only supplemental tags that are mutually exclusive; include a comment in the instructions to make this more clear for the next round of screening

Timeline for next ADME literature update should be similar to last year's: PCBs literature search in September and then a screening for Hazard ID and for ADME in November

## Evidence Map Manuscript – Draft Sections Progress

Health Effect Category	Assigned to	Status
Cardiovascular	Alexander Sergeev (epi), Michal Toborek (tox)	Epi draft delivered on 5/1 and reviewed. Revised epi draft submitted on 5/11 and sent to Michal Toborek. Waiting for Tox draft (ETC: TBD)
Developmental	John Meeker (epi), Aileen Keating (tox)	Draft delivered on 4/17 and reviewed by EPA on 4/22. Revised draft submitted on 5/14.
Endocrine	Michael Bloom (epi), Joanne Trogovich (tox)	Epi: completed, Tox: completed. Draft submitted on 5/8 and reviewed by EPA on 6/5. Revision of Tox component on hold.
Gastrointestinal	Evan Coffman (epi), Brandall Ingle (tox)	Epi: completed, Tox: completed. Draft submitted on 5/7. Review received on 6/3. Revision of Tox component submitted on 6/12.
Hepatobiliary	Evan Coffman (epi), Larry Robertson (tox)	Draft (tox) delivered on 3/9 and reviewed. Final revision in progress.
Immunological	Todd Jusko (epi), Geniece Lehmann (tox)	Waiting for Epi draft (ETC: TBD)
Metabolic	Alexander Sergeev (epi), Michal Toborek (tox)	Epi (rough) draft submitted on 5/18.



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Contract modifications are expected to be fully executed this week and next.

Raquel will follow-up on feedback with Michal Toborek.

Section authors will review new inventories. A couple of the smaller categories have new papers that may draft revisions, but most will only need minor edits.

Very minor edits may be done by EPA, edits requiring more effort may be done by ICF.

## Evidence Map Manuscript – Draft Sections Progress

Health Effect Category	Assigned to	Status
Musculoskeletal	Cynthia Lin (epi), Kelly Shipkowski (tox)	Draft delivered on 4/15 and reviewed by EPA on 4/20. Revised draft submitted on 5/14.
Neurological	Pradeep Rajan & Sharon Sagiv (epi), Pam Lein & Carrie Klocke (tox)	Preliminary epi draft submitted on 5/21, waiting for Tox (ETC: 7/1)
Reproductive	Pam Factor-Litvak (epi) Erin Yost (tox), Xabier Arzuaga (tox)	Waiting for Epi draft male – 6/27; female – TBD

▪ **Completed section drafts:**

- Ocular effects – final draft delivered on 4/15
- Dermal effects – final draft delivered on 4/9
- Respiratory effects – final draft delivered on 5/26
- GI effects – final draft for toxicological component delivered on 6/12

▪ **TO-09/TD-003: new contracts under preparation**

- Additional feedback?

▪ **New literature flow diagram (2015-2017 or 2015-2019)?**



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Pam Lein submitted the neurological effects draft on 7/23.

There have been issues with communication with Pam Factor-Litvak. We're still waiting for her initial draft.

The litflow diagram for the manuscript

## Literature screening & developing inventories

### ■ Tasks included in work plan (v1, approved on 7/10)

1. **Study evaluation (epi neuro studies)**
  - Batch 5 can start as soon as activity under TO-09 is resumed.
2. **Data extraction (neurotox HAWC extractions)** - contractual documentation for Carrie Klocke in preparation; kick-off scheduled for 8/6
3. **Reference tagging in litstream and HERO**
  - **litstream™**
    - Update of outstanding tags (46 studies) completed
    - Re-tagging of references in list sent by EPA in progress (ETC: 8/5)
    - Food consumption analysis - use KAT?
  - **HERO**
    - Waiting for direction from EPA to apply/modify tags
4. **Update documentation and literature flow diagram (Completed)**
  - Revised Hazard ID full-text screening report(2015-2019)
  - Revised literature flow diagram for 2015+2016 (plus short write-up)
  - Literature flow diagram for 2017-2019



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Batch 5 can resume as soon as the contracts with Sharon and Pradeep are finalized. Geniece noted that they should have a similar level of effort on the study evaluation task as Carrie had for the neurotox work. The effort spent in batches 1-4 seems excessive for the worth.

KAT analysis for food consumption studies can proceed.

## Budget, as of 07/24/2020

TO/TD	Budget \$	Budget Hours	Current \$	Current Hours	Cumul. \$	Cumul. Hours	Remain. \$	Remain. Hours
TO-34								
Total								
Tasks 1&2								
TD-001 (EM)								
TD-002 (ADME)								
TD-003 (MIST)								
TO-37								
TD-003 (WP v1)								

# Ex. 4 CBI

▪ **TO-34:**

- TD-001 – Workplan submitted on 7/29
- TD-002 – Workplan submitted on 7/27, approved
- TD-003 – Workplan to be submitted by 8/5
- 2020 literature update for ADME?

▪ **TO-37/TD-003**

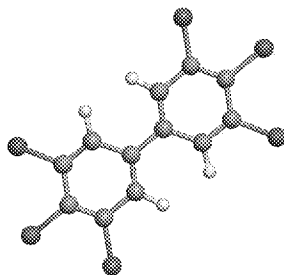
- Workplan approved on 7/10
- 2020 literature search update?



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The 2020 literature search update should be conducted in September/October.



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